EXHIBIT 4

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Via Electronic Mail

James I. McClammy
Jacquelyn Swanner Knudson
Davis Polk & Wardwell, LLP
450 Lexington Avenue
New York, New York 10017

Dear Mr. McClammy and Ms. Knudson:

I would like to begin by thanking the Debtors for their discovery responses of April 24, 2020 (the "Debtors' Responses"). The Debtors' Responses were helpful in assisting in the NAS Ad Hoc Committee's (NASAHC) navigation of the MDL discovery that, inexplicably, the PEC had previously provided to us in a highly inaccessible manner. Notwithstanding, Debtors' Responses are, in several respects, either deficient or spotlight the existence of other documents that are material, relevant and responsive.

By virtue of the fact that the PEC's discovery requests in the MDL regarding medical science focused on the addictive nature of Purdue's products, it is unsurprising that Debtors' Responses lack scientific evidence relevant to the risks presented by fetal opioid exposure. Simply put, the NASAHC seeks qualitatively different, but no less unimportant, scientific evidence than that sought by the PEC.

I. Purdue Response to NASAHC Interrogatories 1-3 and Request for Production 1 and 4.

NASAHC Interrogatories 1-3 and Requests for Production 1-3 seek scientific studies (the "NASAHC Requests"). Debtors responded to these discovery requests by directing us to Purdue's MDL discovery responses and, as you know, Debtors specifically directed us to Purdue's MDL Supplemental Responses of October 5, 2018 and March 4, 2019 (respectively, "Purdue's First Supplemental Response" and "Purdue's Second Supplemental Response").

Purdue's First Supplemental Response to MDL Interrogatory 2 provides a list of bates ranges of scientific studies connected to Purdue's New Drug Application files for OxyContin, Hysingla ER and Butrans; Purdue supplemented this response on March 4, 2019 (the Second

Supplemental Response). For example, the bates-range beginning at PURCHI-000021124 and ending at PURCHI-00326096 comprises tens of thousands of pages and, accordingly, we request additional coding of these bates ranges, including dates, authors, and descriptions of included documents due to the overbroad nature of this response coupled with the unwieldy nature of the MDL database. The second deficiency of note is the request explicitly asks for "a description of ***all*** toxicological, pharmacological, pharmo-kinetic, longitudinal or other scientific study of opioids conducted on animals in your possession" but the Debtors' Response states that production is limited to only "such documents that could be found in its New Drug Application ("NDA") files for OxyContin, Hysingla DR and Butrans." Purdue's Second Supplemental Response (to the MDL Supplemental Response to MDL Interrogatory 2) is similarly lacking pilot studies and dose-ranging studies that either Purdue or Mundipharma may have undertaken for Oxycontin™, oxycodone or hydrocodone in advance of conducting the studies that eventually found their way into the NDA files. We renew our request for production of all pilot studies, dose-ranging studies, or other studies concerning reproductive toxicity, genotoxicity, mutagenicity, teratogenicity or fetal opioid exposure.

NASAHC has identified the following studies that are responsive to our discovery requests but we could not locate them in the MDL Discovery database. We ask that you provide these studies, along with any related pilot studies or dose-ranging studies, or their respective bates ranges:

1. Oxycodone

a. DSE-151- In Vitro Chromosomal aberration
b. DSE-060- Reproductive (embryo-fetal—Segment II) Range-Finding Study- Rat
c. DSE- 061- Reproductive (embryo-fetal—Segment II)- Rat
d. DSE-058- Reproductive (embryo-fetal—Segment II) Range-Finding Study- Rabbit
e. DSE-059- Reproductive (embryo-fetal—Segment II)- Rabbit

2. Naloxone

a. Rat (KPC/30/85)
b. Rabbit (KPC/31/85
c. Rat (KPC/33/85)
d. Rabbit (KPC/35/85)
e. KPC/70/8409
f. KPC/74/8506
g. KPC/71/8409
h. KPC/75/8506
i. N003003A
j. N003003C

Purdue's First Supplemental Responses to MDL Interrogatory 29 lists scientific research that Purdue relied upon for purposes of marketing statements related to eight different topics. Operating in reliance that the list provided is exhaustive the response seemingly satisfies NASAHC Interrogatories 1 and 2, to the extent they report upon the eight topics addressed in MDL Interrogatory 29; notwithstanding, for avoidance of any doubt NASAHC reserves the right

to seek further inquiry on this subject whenever proper. The list, however, fails to satisfy Interrogatory 3 and NASAHC Requests 1-2 because none of the eight topics listed in MDL Interrogatory 29 address "genotoxicity, teratogenic, mutagenic or developmental impacts of in utero exposure". We ask that you revisit your responses to NASAHC by: 1) conducting a unlimited search to find all studies which Purdue relied upon for marketing statements and FDA disclosures related to pregnancy, fetal opioid exposure, and the "genotoxicity, teratogenic, mutagenic or developmental impacts of in utero exposure", and 2) conducting a search to determine if any of the following studies are within Purdue's possession:

1. Broussard C, Rasmussen SA, Reefhuis J et al (2011) Maternal treatment with opioid analgesics and risk for birth defects. Am.J.Obst.Gynecol. 204: 314 e1-11.
2. Chen Q, Cui J, Zhang Y, Yu LC. Prolonged morphine application modulates Bax and Hsp70 levels in primary rat neurons. Neuroscience letters. 2008;441(3):311-4.
3. de Castro A, Jones H E & Johnson R E et al. Methadone, Cocaine Opiates and Metabolite Disposition in Umbilical Cord and Correlations to Maternal Methadone Dose and Neonatal Outcomes. Ther Drug Monit. 2011; 33(4): 443–452.
4. Jacobsen MD, Weil M, Raff (1997) Programmed cell death in animal development. Cell 88 347-54.
5. Kerr JF, Wyllie AH, Currie A R (1972) Apoptosis: A basic biological phenomenon with wide ranging implications in tissue kinetics. British Journal of Cancer. 26: 239-57.
6. Mazarakis ND, Edwards AD, Mehmet H (1997) Apoptosis in neural development and disease. Archives of diseases in childhood. 77 F165-F170.
7. Matsuo A and Kast A (1995) 2 decades of control Himalayan rabbits—reproductive parameters and spontaneous abnormalities in Japan. Lab Matsuo A and Kast A (1995) 2 decades of control Himalayan rabbits—reproductive parameters and spontaneous abnormalities in Japan. Laboratory Animals 29 78-82 oratory Animals 29 78-82.
8. Saxen I. The association between maternal influenza, drug consumption and oral clefts. Acta Odontol Scand.1975;33(5):259–267.

II. <u>Purdue Response to NASAHC Interrogatory 4.</u>

NASAHC Interrogatory 4 seeks information regarding "any case report that details, discloses or otherwise describes any clinical observations of children exposed to opioids in utero" to which you responded by directing us to the NDA Files, Adverse Event Reports (PPLP004385541 through PPLP004390686) and the MedWatch Reports. This response is substantially satisfactory but, for the avoidance of any doubt, we would request that you: 1) provide a bates list of the relevant MedWatch Reports and 2) certify that no other responsive Adverse Event Reports exist other than the ones previously identified.

III. <u>Purdue Response to NASAHC Interrogatory 5.</u>

The NASAHC seeks no further information pursuant to this Interrogatory at this time, but respectfully reserves all rights to request production of additional information whenever proper.

IV. <u>Purdue Response to NASAHC Request for Production 2.</u>

NASAHC's Request for Production 2 explicitly seeks production of "all emails, memo, presentations, white papers or other documents related to your response to Interrogatories Nos. 1, 2, and 3". You were correct in your prediction that the direction provided by your response did enable our review team to hone in on many emails, memos, presentations, white papers and other documents related to fetal opioid exposure. Accordingly, the NASAHC is narrowing this specific request to all emails, memos, presentations, white papers and other materials related to the below-listed documents (items 1-6), together with the full name of the author(s), recipient(s), custodian(s), and date and purpose of each. Please provide any and all draft versions, final versions and published versions of each listed document. Also, please provide any and all memos, emails, internal reports, communications with regulators (federal, state, foreign) or other information that refers or relates to the below-listed documents.

When reviewing these documents you will find, as we did, that several documents are assigned a bates number beginning with the letter "E", and contain unformatted or extracted text of documents for which the full document images are presumably to be found elsewhere within Purdue's document production in the MDL. We would ask that for all documents that bear a bates-stamp beginning with the letter "E" Debtors provide either the bates ranges in entirety and/or copies of the full document images that correspond to the below-listed bates ranges.

1. E01-00002130

2. E513-00026227

3. E513-00046100

4. PPLP004390587

5. PPLP0020000932831

6. PPLPCO20000932832

Regarding E513-00046100, please provide the following additional information:

a. The document states "English version of the amended proposal for a Swedish SmPC". What is the identity of the Swedish SmPC referenced in the document?

b. Please provide any and all scientific evidence, literature or studies in Purdue's possession that supports the following deleted passage from Section 4.6- *"There is no experience of therapy during pregnancy. In animal studies deformities and other embryotoxic effects have been seen at high doses. The clinical relevance of these findings is not known. During pregnancy hydromorphone should be given only on strict indications and when the needs to the mother has been weighed against the risk to the child… Animal studies have shown reproduction toxicological effects of hyrdropmorphone. See 5.3 The risk for human is unknown."*

c. Please provide any and all scientific evidence, literature or studies in Purdue's possession that supports the following deleted passage from Section 5.3- *"Like other opioids hydromorphone causes chromosomal aberrations in in-vitro studies… Studies on*

pregnant animals suggest that hydromorphone has a teratogen potential. If hydromorphone weas given during late pregnancy, increase mortality and reduced birth weight of the off-spring were seen."

V. <u>Purdue Response to NASAHC Request for Production 3.</u>

NASAHC Request for Production 3 asked Purdue to perform a series of word searches. We renew our request that you run the searches previously listed, in addition to the following terms: "Chiari", "septal", "ankyloglossia", "congenital brain damage", "craniosynostosis", "dysplasia", "gastroschisis", "Pierre Robin", "respiratory tract malformation".

Please let us know your availability for a call on **August 13, 2020 at 4:30 p.m. eastern** to discuss these matters further and, in the meantime, we will continue our searches within the PEC's MDL Database.

Very truly yours,

<u>/s/ Scott S. Markowitz</u>

Scott Markowitz

cc: Kevin Thompson
Don Creadore
Scott Bickford
Kent Harrison Robbins
Harold D. Israel
Arik Pries
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